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- (71) Applicant (for all designated States except US): AP-PLIED RESEARCH SYSTEMS ARS HOLDING N.V. [NL/NL]; Pietermaai 15, Curacao (AN).

- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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[NI/NL]: Pietermaal 15, Curacao (AN).

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(75) Title: NOVEL NOTCH-LIKE POLYPEPTIDES

(76) Abstract: The present invention discloses open reading frames (ORFs) in human genome encoding for novel notch-like polypeptides, and reagents related thereto including variants, mutants and fragments of said polypeptides, as well as ligands and antagonists directed against them. The invention provides methods for identifying and making these molecules, for preparing polypeptides, and reagents related thereto including variants, mutants and fragments of said polypeptides, as well as ligands and antagonists directed against them. The invention provides methods for identifying and making these molecules, for preparing pharmaceutical compositions containing them, and for using them in the diagnosis, prevention and treatment of diseases.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NOTCH-LIKE POLYPEPTIDES

(57) Abstract: The present invention discloses open reading frames (ORFs) in human genome encoding for novel notch-like polypeptides, and reagents related thereto including variants, mutants and fragments of said polypeptides, as well as ligands and antagonists directed against them. The invention provides methods for identifying and making these molecules, for preparing pharmaceutical compositions containing them, and for using them in the diagnosis, prevention and treatment of diseases.



INTERNATIONAL SEARCH REPORT

International Application เขบ 03/50968

A. CLASSIFICATION OF SUBJECT MA IPC 7 CO7K14/47 C12N15/62

C12N15/12

C12P21/00

A61K38/17

According to International Patent Classification	(IPC)	ar to	both	national	classification	and I	PC
According to International Patetti Classification	(" U	,					

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) I PC $\,\,7\,\,\,\,\,$ C07 K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search

Category °	ENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	EP 1 447 413 A (RES ASS FORBIOTECHNOLOGY) 18 August 2004 (2004-08-18)	1-6,11, 13-23, 36,37, 39-41
	seq.id.203 -& DATABASE EMBL EMBL; 23 August 2004 (2004-08-23), XP002296518 retrieved from EBI accession no. CQ849734 Database accession no. CQ849734 abstract	
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Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
 Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed 	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
15 September 2004	13. 10. 2004
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer De Kok, A

INTERNATIONAL SEARCH REPORT

International App	
EP 03	/50968

C.(Continua	ation) DOCUMENTS CONS. ERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 2003/100005 A1 (DIAGANA THIERRY TIDIANE ET AL) 29 May 2003 (2003-05-29)	1-6,11, 13-23, 36,37, 39-41
	page 25 - page 29 page 40 - page 44 page 32	
Ρ,Χ	EP 1 347 046 A (RES ASS FOR BIOTECHNOLOGY) 24 September 2003 (2003-09-24)	1-6,11, 13-23, 36,37, 39-41
	seq.id.no.907	
	-& DATABASE EMBL EMBL; 15 December 2003 (2003-12-15), XP002296519	
	retrieved from EBI accession no. AX833783 Database accession no. AX833783 abstract	
X	WO 02/072771 A (CURAGEN CORP) 19 September 2002 (2002-09-19)	1-6,11, 13-23, 36,37, 39-41
	page 213 - page 217	
x	WO 00/58473 A (CURAGEN CORP) 5 October 2000 (2000-10-05)	1-6,11, 13-23, 36,37, 39-41
	page 723	
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Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Although claims 28, 31, 32, 35 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds
2. X	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: See FURTHER INFORMATION sheet PCT/ISA/210
з. 🔲	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remai	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 28, 31, 32, 35 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds

Continuation of Box I.2

Claims Nos.: 7-10, 12, 24-26 completely and 13,19, 23, 27-35, 38, 41 partly

Claims relating to antagonists (claim 7), ligands (claims 8-10), peptide mimetics (claim 12) or to compounds which either enhance or decrease the expression of the polypetides of claims 1-4 (claims 24-26) as well as claims referring thereto have not been searched since NONE of such compounds have been disclosed in technical (structural) terms in the application making a meaningfull search impossible.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Patent document

Publication

	Application No 03/50968
Patent family member(s)	Publication date
1447413 A2	18-08-2004
03046139 A2	05-06-2003
1347046 A1 2004008216 A	24-09-2003 15-01-2004

cited	d in search report	1	date		member(s)		date	
EP	1447413	Α	18-08-2004	EP	1447413	A2	18-08-2004	
US	2003100005	A1	29-05-2003	WO	03046139	A2	05-06-2003	٠
EP	1347046	Α	24-09-2003	EP	1347046		24-09-2003	
				JP US	2004008216 2004005560		15-01-2004 08-01-2004	
wo	02072771		19-09-2002	US	2003208039		06-11-2003	
				CA	2440108		10-10-2002	
				CA	2440337		19-09-2002	
				CA	2440345		19-09-2002 16-06-2004	
•				EP	1427749		23-06-2004	
				EP EP	1430110 1373526		02-01-2004	
}				WO	02072757		19-09-2002	
ŀ				WO	02072771		19-09-2002	
				WO	02079398		10-10-2002	
				ÜS	2004043382		04-03-2004	
1				ÜS	2004002120		01-01-2004	
1				ÜŠ	2002183205		05-12-2002	
ł				WO	02072770		19-09-2002	
1				US	2003203363	A1	30-10-2003	
]				US	2004018970		29-01-2004	
]				WO	03076578		18-09-2003	
[WO	03083046		09-10-2003	
ŀ				US	2003215449		20-11-2003	
[WO	02070660		12-09-2002	
i				US	2003198957		23-10-2003	
				US	2003207348	A1	06-11-2003	
MO	0058473	Α	05-10-2000	AU	3774500	Α	16-10-2000	
WU	0000470	^	03 10 E000	CA	2383592		05-10-2000	
				EP	1165784		02-01-2002	
1				ĴΡ	2004507202		11-03-2004	
1				WO	0058473	A2	05-10-2000	
1				US	2003198953	A1	23-10-2003	